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10/574,031	06/20/2006	Yuntao Wu	59582(47992)	8029

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EXAMINER	
KINSEY WHITE, NICOLE	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
01/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,031	WU ET AL.	
	Examiner	Art Unit	
	Nicole Kinsey White, PhD	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,22,24,31,35 and 48* is/are pending in the application.

4a) Of the above claim(s) *48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,22,24,31 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/20/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election without traverse of Group I (original claims 1-36) in the reply filed on October 24, 2007 is acknowledged.

Status of the Claims

Claims 20-21, 23, 25-30, 32-34, 36-47 and 49-71 have been cancelled. Claims 1-19, 22, 24, 31, and 35 are currently under examination. Claim 48 (Group II) has been withdrawn as being directed to a non-elected invention.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because it does not identify the citizenship of each inventor. The citizenship for Yuntao Wu is absent.

Specification

The disclosure is objected to because of the following informalities: The specification contains blanks at pages 5, 6, 14, 15 and 16.

Appropriate correction is required.

Claim Objections

Claims 10, 11, 14 and 15 objected to because of the following informalities: Claims 10 and 11 refer to figures. According to section 2173.05(s) of the MPEP, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim".

Claim 14 recites improper Markush language. The word "and" should be inserted after (CAT).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 35 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that a specific host cell is required to practice the claimed invention. As such, the host cell must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so

obtainable or available, the requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the host cell.

The host cells disclosed in the specification do not appear to be produced from a repeatable process, and it is not apparent if the host cells are both known and readily available to the public. It is noted that pages 6, 14, 15 and 16 of the specification indicates that the host cells have been deposited; however, there is no indication in the specification as to deposit number or public availability.

If the deposit was made under the terms of the Budapest Treaty, then a statement, affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, or someone empowered to make such a statement, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement.

If the deposit was not made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CRF 1.801-1.809 and MPEP 2402-2411.05, applicants may provide assurance of compliance by statement, affidavit or declaration or by someone empowered to make the same or by a statement by an attorney of record over his or her signature and registration number showing that:

(a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claim is drawn to, *inter alia*, an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of: SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3; or a complement thereof, or a sequence which is at least about 60% identical to a nucleic acid sequence selected from the group consisting of: SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3; or a, complement thereof.

The written description rejection is made because the claims are interpreted as being drawn to a genus of nucleic acid molecules "at least about 60% identical" to a nucleic acid sequence selected from SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3. The applicable standard for the written description requirement can be found in MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written

Description Guidelines; Enzo Biochem Inc. v. Gen-Probe Inc., 63 USPQ2d 1609; Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CAFC 2004). To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3. There is no disclosure of any particular portion of the structure that must be conserved or that can be altered in order to be "at least about 60% identical" to a nucleic acid sequence selected from SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3.

The specification discloses at pages 18 and 19 how to determine the percent identity of two nucleic acid molecules. However, the specification does not indicate which portions of SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3 are essential or which portions of SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3 can be modified or altered.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

The court clearly states in Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for

purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented what is claimed. As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acid molecules that are "at least about 60% identical" to SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3. Given that the specification has only described the structures of SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3, the full breadth of the claims does not meet the written description provision of 35 U.S.C. 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 recites the limitation "the luciferase" in reference to claim 15. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 13, 14, 16, 17, 18, 24 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Saiga et al. (U.S. Patent No. 6,090,783).

The claims are directed to an isolated nucleic acid molecule comprising:

a) a promoter, wherein the activity of the promoter is dependent on the presence of the human immunodeficiency virus (HIV) Tat protein;

b) at least one splice donor site and at least one splice acceptor site;

c) an expressible sequence which is not a wild-type HIV sequence, wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site; and

d) a Rev Responsive Element (RRE) from the human immunodeficiency virus, wherein elements (a)-(d) are operably linked; or a complement thereof.

Saiga et al. discloses a gene expression vector comprising a) a promoter, which can be the HIV 5'-LTR, wherein the activity of the promoter is dependent on HIV Tat (see col. 4, lines 4-5; col. 8, lines 57-65; and col. 24, line 63 to col. 25, line 17), b) at least one splice donor site and at least one splice acceptor site (see figure 9 and col. 24, line 63 to col. 25, line 17), c) an expressible non-wild type HIV sequence (e.g., a therapeutic gene, which can be toxic; a reporter gene such as CAT, luciferase, etc.) located between the splice donor and splice acceptor (see col. 4, lines 6-9 and col. 8, line 66 to col. 9, line 17), and d) an RRE from HIV (see col. 9, lines 18-28), wherein the elements are operably linked (see figure 9). The construct can be cloned into an expression vector and transfected into a host cell (see col. 8, lines 47-56).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4-9 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saiga et al. (U.S. Patent No. 6,090,783) as applied to claims 1, 2, 13, 14, 16, 17, 18, 24 and 31 above.

The claims are drawn to the isolated nucleic acid construct described above wherein the splice donor and acceptor sites are the HIV D1 and HIV A7 donor and acceptor sites, respectively.

The choice and placement of splice donors and acceptors within a construct is well within the purview of one of ordinary skill in the art. Therefore, it would have been obvious to one of ordinary skill in the art to select HIV splice donors and acceptors

(D1/A7 and/or D4/A5) or any other known splice donor and acceptor to incorporate into the claimed construct and the results would have been predictable. Choosing a particular splice donor and acceptor to include in a construct is routine.

Saiga et al. teaches the use of the CAT and luciferase reporter genes, but not the fluorescent proteins recited in instant claims 15. It is well within the purview of one of ordinary skill in the art to substitute one reporter gene for another and the results would have been predictable.

Claims 1-18, 24 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Corbeau et al. (U.S. Patent No. 6,323,019) in view of Hope et al. (U.S. Patent No. 6,136,597) and D'Costa et al. (Journal of General Virology, 2001, 82:425-434) and as evidenced by Saiga et al.

Figure 8B of Corbeau et al. discloses a gene expression vector (pDM128) comprising a) an SV40 promoter, b) at least one splice donor site and at least one splice acceptor site, c) an expressible non-wild type sequence (i.e., CAT gene) located between the splice donor and splice acceptor, and d) an RRE from HIV, wherein the elements are operably linked (see figure 8B). Figure 8B also discloses the 3'-LTR. The construct of Corbeau et al. can be cloned into a vector (see, for example, pDM128) and transfected into host cells (see, for example, col. 17, line 51 to col. 18, line 9).

Figure 8B of Corbeau et al. does not disclose a 5' HIV LTR, specific HIV splice donor and acceptor sites, a packaging signal, or various reporter and therapeutic proteins to be expressed in the construct. However, Corbeau et al. teaches that many

promoters are useful, including known inducible and constitutive promoters. One preferred promoter comprises the 5' HIV LTR (see col. 4, lines 13-21). Other promoters that can be used include pol III promoters, pol II promoters, or the natural promoters found in an HIV LTR (see col. 6, lines 52-60). In addition, Hope et al. states that when cloning in mammalian cell systems, promoters derived from the genome of mammalian cells or from mammalian viruses (e.g., the retrovirus long terminal repeat; the adenovirus late promoter; the vaccinia virus 7.5K promoter) may be used (col. 13, lines 8-13). Thus, it would have been obvious to replace the SV40 promoter in figure 8B with the HIV 5'-LTR.

The choice and placement of splice donors and acceptors within a construct is well within the purview of one of ordinary skill in the art. Therefore, it would have been obvious to one of ordinary skill in the art to select HIV splice donors and acceptors (D1/A7 and/or D4/A5) or any other known splice donor and acceptor to incorporate into the claimed construct and the results would have been predictable. Choosing a particular splice donor and acceptor to include in a construct is routine.

Further, the inclusion of a packaging signal is also within the purview of one of ordinary skill in the art. It is well known in the art to efficiently transfer lentiviral constructs to other HIV infected cells, packaging signals are necessary to efficiently package the construct into HIV particles, which then go on to infect other cells, thus delivering the therapeutic or cytotoxic protein to other infected cells (see, for example, D'Costa et al.).

Corbeau et al. teaches the use of the CAT reporter gene, but not the fluorescent proteins recited in instant claims 15 and 16 or a therapeutic protein as recited in claims 17 and 18. It is well within the purview of one of ordinary skill in the art to substitute one reporter gene for another or to substitute a therapeutic/toxic gene and the results would have been predictable (see, for example, Saiga et al.).

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Saiga et al. or Corbeau et al. as applied to claim 1 above, and further in view of D'Costa et al. (Journal of General Virology, 2001, 82:425-434).

The claim requires the inclusion of an internal ribosome entry site (IRES) in the construct.

It would have been obvious to one of ordinary skill in the art to modify the construct taught by Saiga et al. or Corbeau et al. to include an IRES, especially if one contemplates a construct with more than one expressible gene product. One would have been motivated to do so given the fact that IRES sequences are routinely used in the art to allow for the independent initiation of translation of a cloned gene. There would have been a reasonable expectation of success given the fact that there are many others who have successfully created constructs that included IRES (see, for example, D'Costa et al.). Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole Kinsey White, PhD whose telephone number is (571) 272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Nicole Kinsey White, PhD
Examiner
Art Unit 1648

/nkw

/Stacy B. Chen/ 1-3-08
Primary Examiner, TC1600